



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER OF PATENTS AND TRADEMARKS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/193,538	11/17/1998	PATRICIA A. BILLING-MEDEL	6193.US.P1	2144

23492 7590 05/27/2003

STEVEN F. WEINSTOCK  
ABBOTT LABORATORIES  
100 ABBOTT PARK ROAD  
DEPT. 377/AP6A  
ABBOTT PARK, IL 60064-6008

EXAMINER
----------

SOUAYA, JEHANNE E

ART UNIT	PAPER NUMBER
----------	--------------

1634

DATE MAILED: 05/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/193,538

Applicant(s)

BILLING-MEDEL ET AL.

Examiner

Jehanne E Souaya

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on 06 March 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 23-37,39,40,42-44,50-54,56-58,60-63,65-70 and 72-78 is/are pending in the application.
- 4a) Of the above claim(s) 23-37,39,40,42-44,50 and 51 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 52-54,56-70 and 72-78 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☒ Interview Summary (PTO-413) Paper No(s). 4/2003.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_. 6) ☒ Other: PTO-413; 5/2003.

### **DETAILED ACTION**

1. Currently, claims 23-37, 39-40, 42-44, 50-54, 56-58, 60-63, 65-70, and 72-78 are pending in the instant application. Claims 23-37, 39-40, 42-44, and 50-51 are withdrawn from consideration as being directed to non elected subject matter from a previous restriction requirement. Claims 55, 59, 64, and 71 have been canceled. Claims 52-54, 56-58, 60-63, 65-70, and 72-78 are currently under examination. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. The following rejections constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is NON-Final.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Claim Objections***

3. Claim 61 is objected to because of the following informalities: the claim is grammatically incorrect. The claim could read: "reacting the test sample with a solid phase". Appropriate correction is required.

#### ***Maintained Rejections***

##### ***Claim Rejections - 35 USC § 101***

4. Claims 52-54, 56-58, 60-63, 65-70, and 72-78 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific or substantial asserted utility, or a well established utility.

The claims are drawn to polynucleotides having a sequence selected from the group consisting of SEQ ID NOS 1-7, to methods of detecting a target polynucleotide using the polynucleotides of SEQ ID NOS 1-7, and to kits comprising these polynucleotides.

The specification teaches the general utility for the invention is detection of the gene product itself in a sample (p. 10 of the specification). This is not deemed to be specific as this utility is applicable to polynucleotides in general. The specification asserts that the polynucleotides of the invention can be used to detect, amplify, or quantify genes, nucleic acids, cDNAs or mRNAs relating to breast tissue disease and conditions associated therewith (p. 25). The specification further asserts that the compositions and methods described in the specification will enable the identification of certain markers as indicative of breast tissue disease or condition wherein this information will aid in, for example, detecting conditions associated with BS274, especially breast cancer (p. 10-11, bridging paragraph). However this is assertion is not deemed to be substantial as the specification does not teach the specific role of BS274 in breast cancer, nor has the specification demonstrated that BS274 is a marker for breast disease, especially breast cancer. From the teachings in the specification, it is evident that neither the function nor the role of BS274 in association with breast disease or breast cancer was known at the time the invention was filed. At page, 11, lines 6-12, the specification states "It is also thought that the polynucleotides or polypeptides and protein encoded by the BS274 gene are useful as a marker. This marker is either elevated in disease such as breast cancer, altered in disease such as breast cancer, or present as a normal protein but appearing in an inappropriate body compartment." The specification only teaches that the BS274 consensus sequence was found more than 28 more times in breast tissue libraries than non breast tissue libraries (p 54), but does not demonstrate

Art Unit: 1634

that BS274 is a marker for breast cancer (analysis to follow). Therefore, while the BS274 consensus sequence is found to be present to a greater extent in breast tissue, this is not considered a "real world" use for the claimed polynucleotides, kits, or methods of using the polynucleotides of the claimed invention. Further experimentation would be required to determine whether the elevated presence of the BS274 consensus sequence, whether the presence of altered BS274, or whether the presence of BS274 in an inappropriate body compartment is indicative of breast disease or breast cancer. The specification also does not provide any teachings as to the function of the protein encoded by BS274.

At page 54, the specification teaches that ESTs were derived from cDNA libraries made from breast tumor tissues, breast non-tumor tissues and numerous other tissues, both tumor and non tumor and entered into a database. The specification teaches that the transcript images were evaluated to identify ESTs that were representative primarily of breast tissue libraries, and that these ESTs were ranked, giving an EST corresponding to the consensus sequence of BS274 (SEQ ID NO 7) which was found in 23% of breast tissue libraries (p. 62). The specification teaches that the consensus sequence (SEQ ID NO 7) or fragments thereof (SEQ ID NOS 1-6) were found more than 28 more times in breast than non breast tissues. However, while the consensus sequence expression appears to be more prevalent in breast tissue, the specification has not demonstrated that BS274 is specific for breast tumor tissue. The specification only teaches that the BS274 consensus sequence was found 28 more times in breast than non breast libraries, but does not teach the ratio of BS274 in normal breast vs. breast tumor tissues. Thus while the specification suggests that SEQ ID NOS 1-7 can be used to detect nucleic acids relating to breast tissue disease the specification does not demonstrate such. Furthermore, at

page 62, the specification teaches upon hybridization with a BS274 probe, northern analysis revealed an approximately 860 nucleotide band in the RNA of 5 out of 5 normal breast tissue samples was found. While the specification also teaches that the band was found in 2 of 2 breast cancer tissue samples, the specification does not teach whether a difference in expression levels was found between breast cancer tissue and non breast tissue. Thus while the specification suggests that SEQ ID NOS 1-7 can be used to detect nucleic acids relating to breast tissue disease the specification does not demonstrate such.

***Claim Rejections - 35 USC § 112***

***Enablement***

5. Claims 52-54, 56-58, 60-63, 65-70, and 72-78 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The specification teaches that the compositions and methods described herein will enable the identification of certain markers as indicative of a breast tissue disease or condition, and that the information obtained therefrom will aid in the detecting, diagnosing, staging, monitoring, prognosis, in vivo imaging, preventing or treating diseases of the breast, however the specification does not teach having done so. However, it cannot be determined from the teachings in the specification, and the art is silent as to, what the biological function of the polypeptides encoded by the sequences of SEQ ID NOS 1-7 and also as to how these polynucleotides or polypeptides are correlated to or would be useful in detecting any breast tissue diseases. Therefore, the skilled artisan would have to

Art Unit: 1634

perform undue experimentation to determine the function of the polypeptides encoded by the sequences of SEQ ID NOS 1-7 or to determine whether the presence of these polynucleotides is associated with breast cancer or any breast disease.

### ***Response to Arguments***

The response traverses the rejection. The response asserts that as discussed in Example 1, EST's corresponding to the consensus sequence of BS274 were found 28 times more in breast tissue than non breast tissue libraries. This argument has been thoroughly reviewed but was unpersuasive as tissue specific expression is not considered a specific, substantial, or well established utility. The disclosure that EST's corresponding to the consensus sequence of BS274 were found 28 times more in breast tissue than non breast tissue libraries does not indicate that BS274 expression of BS274 can be used to diagnose breast cancer because neither the specification, nor any of applicant's responses, provide a comparison between expression of BS27 in breast tumor vs. normal breast expression. The response asserts that the specification teaches that there is a need in the art for the identification of new markers that can be used in the diagnosis, monitoring and treatment of patients suffering from breast disease, particularly breast cancer and that markers could be used to monitor for the elevated expression of such markers in inappropriate body compartments. The response asserts that the identification of such outside the normal host tissue would indicate breast disease and cites PSA and CEA as examples of markers that are normal components of seminal fluid and the inner lining of the colon, respectively, but that are present in markedly elevated amounts in the blood of patients with prostate and colon cancers respectively. The response asserts that BS274 is similar to PSA and CEA and that the usefulness of elevated levels of PSA and CEA in the blood of patients with

Art Unit: 1634

cancer demonstrates the utility of tissue specific markers. This argument has been thoroughly reviewed but was found unpersuasive. Firstly, although some tissue specific markers whose elevated presence in blood is indicative of certain specific forms of cancer, the same cannot be said for tissue specific markers in general. The art does not teach or demonstrate such as a well established utility for tissue specific markers in general. Secondly, neither the specification nor the gel submitted in applicant's 9/17/2001 response demonstrate that BS274 is elevated in the blood or an inappropriate body compartment of patients with breast disease or breast cancer. Further experimentation would be required of the skilled artisan to determine if elevated levels of BS274 in a patient's blood or an inappropriate body compartment was indicative of breast disease in general, or specifically breast cancer. However, as noted by *Brenner v. Manson*, 383 US 519, 535-536 (1996), "Congress intended that no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use - testing... a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

The response asserts that Figure 1 (the gel submitted in applicant's 9/17/2001 response) which is a result of an RT-PCR assay designed to demonstrate the utility of BS274 as a marker that can help identify a Tumor of Unknown Primary Origin. The response asserts that tumors of unknown origin are a huge medical problem and further cites page 2537 of *Cancer Principles & Practices of Oncology* as support for such utility. This argument as well as the gel submitted by applicants designated as Figure 1 have been thoroughly reviewed but were found unpersuasive. With regard to the reference cited by the response, as the examiner could not obtain a copy of the reference (no copy was provided with the response, applicant's representative was unable to provide a copy for the examiner, and no year or edition was cited with regard to the reference



Art Unit: 1634

which prevented the Office's library from obtaining a copy), the examiner is unable to consider applicant's arguments with regard to such. With regard to the gel provided in applicant's 9/17/2001 response, the instant response asserts that the gel's showing of a lack of expression of BS274 in non – breast cancers illustrates the specificity of BS274 as a marker to establish the origin of a tumor of unknown primary origin. The response further asserts that in addition, since BS274 is not expressed in normal peripheral blood lymphocytes, that BS274 could be used as a tumor cell detection marker, like PSA. These arguments have been thoroughly reviewed but were found unpersuasive as neither the specification nor the gel teach or demonstrate that BS274 is expressed in the blood or an inappropriate body compartment of patients with breast cancer such that BS274 could be used to indicate the origin of tumors of unknown primary origin or be used as a tumor cell detection marker. As stated previously, further experimentation would be required of the skilled artisan to determine if elevated levels of BS274 in a patient's blood or an inappropriate body compartment was indicative of breast disease in general, or specifically breast cancer. However, as noted by *Brenner v. Manson*, 383 US 519, 535-536 (1996), "Congress intended that no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use - testing... a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

The response asserts that the examiner has failed to set forth factual reasons that would lead one skilled in the art to question the objective truth of the statement of operability of the present invention. This argument has been thoroughly reviewed but was found unpersuasive. In the rejection reiterated above, the examiner set forth that the specification did not set forth either a specific or substantial utility for the presently claimed invention. The examiner provided

evidence from the specification for such rejection. To reiterate: The specification teaches the general utility for the invention is detection of the gene product itself in a sample (p. 10 of the specification). This is not deemed to be specific as this utility is applicable to polynucleotides in general. The specification asserts that the polynucleotides of the invention can be used to detect, amplify, or quantify genes, nucleic acids, cDNAs or mRNAs relating to breast tissue disease and conditions associated therewith (p. 25). The specification further asserts that the compositions and methods described in the specification will enable the identification of certain markers as indicative of breast tissue disease or condition wherein this information will aid in, for example, detecting conditions associated with BS274, especially breast cancer (p. 10-11, bridging paragraph). However this assertion is not deemed to be substantial as the specification does not teach the specific role of BS274 in breast cancer, nor has the specification demonstrated that BS274 is a marker for breast disease, especially breast cancer. From the teachings in the specification, it is evident that neither the function nor the role of BS274 in association with breast disease or breast cancer was known at the time the invention was filed. At page, 11, lines 6-12, the specification states "It is also thought that the polynucleotides or polypeptides and protein encoded by the BS274 gene are useful as a marker. This marker is either elevated in disease such as breast cancer, altered in disease such as breast cancer, or present as a normal protein but appearing in an inappropriate body compartment." The specification only teaches that the BS274 consensus sequence was found more than 28 more times in breast tissue libraries than non breast tissue libraries (p 54), but does not demonstrate that BS274 is a marker for breast cancer. Therefore, while the BS274 consensus sequence is found to be present to a greater extent in breast tissue, this is not considered a "real world" use for the claimed polynucleotides, kits, or

Art Unit: 1634

methods of using the polynucleotides of the claimed invention. While the response asserts that BS274 could be used to determine the origin of tumors of unknown primary origin, this utility was not asserted or demonstrated in the specification as originally filed and the prior art fails to provide support that tissue specific markers generally were used to indicate the origin of tumors of unknown primary origin or that such was a well established utility at the time the application was filed. Therefore, the rejections under 35 USC 101 and 112/first paragraph are maintained.

***New Grounds of Rejection***

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(f) he did not himself invent the subject matter sought to be patented.

7. Claims 67-70 are rejected under 35 U.S.C. 102(a) as being anticipated by Incyte LifeSeq™ Database (see specification at page 54, line 30, and page 55 lines 9-10).

As applicants have asserted in the specification, the nucleic acid clones for the sequences of SEQ ID NOS 1-5, (3107759H1, 604775H1, 1996033H1, g3178059, g2355479) were procured from, and therefore known and used by, Incyte Genomics at the time the invention was filed. It is noted that the nucleotide sequence is an inherent property of the nucleic acid clones. Therefore

Art Unit: 1634

polynucleotides having SEQ ID NOS 1 -5, as well as those that could be produced by either recombinant techniques or synthetic techniques were known and used in the art at the time of filing of the instant application.

8. Claims 67-70 are rejected under 35 U.S.C. 102(b) based upon a public use or sale of the invention.

As applicants have asserted in the specification, the nucleic acid clones for the sequences of SEQ ID NOS 1-5, (3107759H1, 604775H1, 1996033H1, g3178059, g2355479) were procured from, and therefore known and used by, Incyte Genomics at the time the invention was filed. It is noted that the nucleotide sequence is an inherent property of the nucleic acid clones.

9. Claims 60-62, and 65 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

As applicants have asserted in the specification, the nucleic acid clones for the sequences of SEQ ID NOS 1-5, (3107759H1, 604775H1, 1996033H1, g3178059, g2355479) were procured from, and therefore known and used by, Incyte Genomics at the time the invention was filed. It is noted that the nucleotide sequence is an inherent property of the nucleic acid clones.

#### ***Claim Rejections - 35 USC § 103***

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 65 and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Incyte LifeSeq™ Database (see specification at page 54, line 30, and page 55 lines 9-10), in view of Ahern, Holly (The Scientist, vol. 9, 1995, from the Internet, pages 1-5).

As applicants have asserted in the specification, the nucleic acid clones for the sequences of SEQ ID NOS 1-5, (3107759H1, 604775H1, 1996033H1, g3178059, g2355479) were procured from, and therefore known and used by, Incyte Genomics at the time the invention was filed. Although the nucleic acid clones are not taught in kit format, Ahern teaches that offering reagents in kit format offers scientists the opportunity to better manage their time and further teaches that buying premade reagents and kits offers scientists a convenience and the ability to save time (see p. 4, first and 2nd para). Therefore, it would have been prima facie obvious to one of ordinary skill the art at the time the invention was made to package the clones in a container for the obvious improvement of making the clones available in a convenient format to researchers.

12. Claims 52, 56-58, 60-63, and 76-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Incyte LifeSeq™ Database (see specification at page 54, line 30, and page 55 lines 9-10), in view of Londos et al (US Patent 5,585,462).

Claims 76-78 are drawn to expression systems and cells transfected with such, comprising the nucleic acids of SEQ ID NOS 1-5. As applicants have asserted in the specification, the nucleic acid clones for the sequences of SEQ ID NOS 1-5, (3107759H1, 604775H1, 1996033H1, g3178059, g2355479) were procured from, and therefore known and used by, Incyte Genomics at the time the invention was filed. Although the nucleic acid clones are not specifically taught as procured in a recombinant expression system or cell comprising such, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to construct an expression system comprising one of nucleic acids of SEQ ID NOS 1-5 to express any proteins encoded by such. Such methods were known in the art at the time of the invention as exemplified by the teachings of Londos, which teaches how transfect a cell with nucleic acids for the purposes of expression protein (col. 14, lines 53-col. 15).

Londos further teaches that the DNA can be directly detected using Southern hybridization with probes that hybridize and detect the DNA (see col. 21, lines 45-50) (claim 52). Londos also teaches that sandwich hybridization can be used to detect the DNA where in the assay utilizes a "capture" nucleic acid covalently immobilized to a solid support and a labeled "signal" nucleic acid in solution which bind to the target DNA (see col. 22, lines 10-30). Londos also teaches using RT-PCR for amplification of RNA sequences (see col. 29, lines 1-2). While Londos does not teach detection of mRNA using RT-PCR and subsequent hybridization and detection with a probe, it would have been prima facie obvious to one of ordinary skill in the art

at the time the invention was made that mRNA could be detected using RT-PCR to produce cDNA and that the cDNA could be detected with a probe specific for the cDNA sequence. Such amplification and detection methods were readily known and practiced at the time of the invention. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the detection methods taught by Londos to detect the sequences of the instantly claimed invention as Londos teaches that such methods can be used to detect nucleic acids in a test sample.

16. Claims 53, 54, 72, and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Incyte LifeSeq™ Database (see specification at page 54, line 30, and page 55 lines 9-10) in view of Londos et al, as applied to claims 52, 56-58, 60-63 above, and further in view of Panadian et al (US Patent 6,306,657; filed Sep. 25, 1996).

As applicants have asserted in the specification, the nucleic acid clones for the sequences of SEQ ID NOS 1-5, (3107759H1, 604775H1, 1996033H1, g3178059, g2355479) were procured from, and therefore known and used by, Incyte Genomics at the time the invention was filed

Londos teaches that the DNA can be directly detected using Southern hybridization with probes that hybridize and detect the DNA (see col. 21, lines 45-50) (claim 52). Londos also teaches that sandwich hybridization can be used to detect the DNA where in the assay utilizes a "capture" nucleic acid covalently immobilized to a solid support and a labeled "signal" nucleic acid in solution which bind to the target DNA (see col. 22, lines 10-30). Londos also teaches using RT-PCR for amplification of RNA sequences (see col. 29, lines 1-2). While Londos does not teach detection of mRNA using RT-PCR and subsequent hybridization and detection with a

Art Unit: 1634

probe, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made that mRNA could be detected using RT-PCR to produce cDNA and that the cDNA could be detected with a probe specific for the cDNA sequence. Such amplification and detection methods were readily known and practiced at the time of the invention.

Although Londos does not teach first attaching the DNA to a solid phase before detection or attaching the probe to a solid support before contacting the DNA to the probe, Panadian teaches that some nucleic acid hybridization assays involve immobilization of the target sequence on a solid support followed by washing the remainder of the reaction mixture (see col. 3, lines 16-24). Panadian teaches that this involves techniques that attempt to either immobilize the target sequence before adding a label probe or using an immobilized labeled probe to capture the target nucleotide sequence. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made that the methods taught by Panadian have been suitable hybridization techniques and could have been used in the methods taught by Londos for the purpose of detecting the sequences of the instantly claimed invention in a test sample. It would have further been prima facie obvious to provide polynucleotides on an array for the obvious improvement of testing for the presence of more than one sequence at a time.

### ***Conclusion***

13. No claims are allowable.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jchanne Souaya whose telephone number is (703) 308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.



Application/Control Number: 09/193,538

Page 16

Art Unit: 1634

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Jehanne Souaya  
Patent examiner  
Art Unit 1634

5/21/03